REMARKS

Reconsideration of this application is requested in view of the amendments to the specification and claims and the remarks presented herein.

Applicants' attorney wishes to thank the Examiner in charge of the application for the courtesies extended to him at the interview on April 29, 2003 at which time, the rejection of February 24, 2003 was discussed.

The claims in the application are claims 3 to 9, 13, 18 to 28 and 30 to 32, all other claims having been cancelled.

Claim 18 was rejected under 35 USC 112, second paragraph as being indefinite in the use of the term "derivatives". The present amendment removes the expression from the claims and therefore, this ground of rejection is obviated.

All of the claims were rejected under 35 USC 112, first paragraph, as not being enabling for the scope of the claims. The Examiner objected to "estradiol derivatives" and "conjugated equine estrogens" and "cardiovascular disorders" as well as "prevention of osteoporosis". The Examiner was of the opinion that undue experimentation would be necessary to ascertain the invention.

Applicants respectfully traverse these grounds of rejection since it is believed that the amended claims are clearly enabling in their present scope. The reference to "cardiovascular disorders" has been deleted and "estrogen deficiencies" and "osteoporosis" are well known and Applicants are submitting herewith pages 3302 through 3312 of the Physicians Desk Reference which clearly points out what is meant by the use of estradiol and the various progestins for the treatment of osteoporosis and estrogen deficiencies and therefore, this is well understood by those skilled in the art. The claims are limited to17β-estradiol or esters thereof and nomegestrol acetate. It is well known to those skilled in the art that the esters are hydrolyzed by the body so as to have as the active ingredient estradiol and nomegestrol acetate and the claims clearly recite the active dosages on a continual basis "per daily dose" has been added to the claims for clarity. Therefore, the specification is clearly enabling for the present invention and withdrawal of this ground of rejection is requested.

All of the claims were rejected under 35 USC 103 as being obvious over the Plunkett et al and Blanc et al references. Both the references allegedly teach the art which embraces the instantly claimed invention. The Examiner states that Plunkett et al teaches a method of hormonal treatment for menopausal disorders involving continuous administration of progestins and estrogens and the Blanc et al reference allegedly discloses continuous hormone replacement therapy combining nomegestrol acetate and a gel patch or oral estrogen and the Examiner deems that the invention would be obvious therefrom.

Applicants respectfully traverse this ground of rejection since it is deemed that the neither of the references anticipates or renders obvious Applicants' invention. The present invention is an improvement over that described in copending parent application Serial No. 09/284,147. The French equivalent to this application is discussed on page 10 of the present application and it shows that surprisingly, the present invention is an improvement over that of the copending application. The invention described therein uses 1.5 to 3.75 mg of nomegestrol acetate and the clinical trials on a broader scale have now shown that the present invention is useful at much lower dosages of nomegestrol acetate, namely, 0.3 to 1.25 mg which can be effective with still greater safety because of the lower dosages. The Examiner's attention is directed to the comparative examples set forth in the application as filed, particularly Tables 1, 2 and 3 which also compares the Plunkett et al reference with the present invention which clearly demonstrates the unexpected advantages thereof. Applicants are submitting herewith a copy of a declaration which is being filed in the parent application and clearly demonstrates that the nomegestrol acetate is completely different from that of the Plunkett et al reference and the progestins are in no way related. The Plunkett et al reference was discussed with the Examiner at the interview on November 14, 2001 and Applicants call the Examiner's attention to the arguments presented in the amendment of December 18, 2001 with respect to the distinctions over the Plunkett et al reference.

With respect to the Blanc et al reference, this also does not teach Applicants' invention since it relates to administration of 2.5 mg per day of nomegestrol acetate with 1.5 mg per day of 17β-estradiol percutaneously or 50 μg per day of 17β-estradiol administered by a transdermal patch and 2 mg per day of estradiol orally administered. Thus, the amount of nomegestrol acetate disclosed in the reference is more than double that of the present invention and therefore, it does not teach the advantages of a low dosage of nomegestrol acetate as Applicants have found. It does not teach the advantages of a low dosage of nomegestrol acetate as Applicants have found, that is to say the dissociation between secretory effect (progestative activity) and atrophic effect (anti-estrogenic activity), which can only be observed in the claimed lower dose. To obtain such a atrophying effect, a man stilled in the art, with the teacing of the Blanc et al document would have increase the dosage of nomegestrol acetate but would never have used nomegestrol acetate in a lower dose, as described in the present invention. Moreover, the data presented shows an overall rate of cycles with no bleeding of 60% for the oral administration which was slightly poorer than with the other preparations as pointed out on page 907.

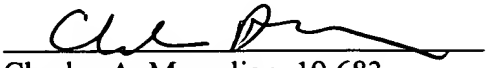
Applicants are submitting herewith a copy of Dr. Thomas' declaration filed in the copending application Serial No. 09/284,147 on which the present invention is an

improvement over. The original declaration has been submitted in the application and it clearly points out the advantages of the use of the present invention over the references cited by the Examiner therein and cited in this application as well particularly with respect to the Plunkett et al patent. It is believed that the claims clearly define the invention thereover and withdrawal of all of the prior art rejections is requested.

With respect to the Examiner's rejection based on 35 USC 112, first paragraph, as not being enabling for the present claims, it is deemed that the Examiner is incorrect. The claims are directed only to the use of nomegesterol acetate and its esters together with estradiol, esters of estradiol or estrogen conjugated equine estrogens. These are well illustrated by the use of estradiol and estradiol valerate and by nomegesterol acetate and its acetate. Therefore, the specification is enabling for the present scope of the claims. With respect to the conjugated equine estrogens, these are known to fall into the same therapeutic class and they have equivalent effects on the reproductive system and menopause symptoms, Applicants are submitting herewith a copy of an article entitled Estrogen Replacement and Coronary Heart Disease by Barret-Conner et al. Equine conjugates estrogens are known by the trademark Premarin and is of a known composition and can probably be described as a generic term for the product and a representative dose is given in the applications as filed. Therefore, the claims are believed to be fully enabled by the present disclosure and withdrawal of this ground of rejection is requested.

In view of the amendments to the specification and claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
Muserlian, Lucas and Mercanti



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